HIV vaccine strategy expands immune responses

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Mosaic vaccines show promise in reducing the spread of deadly virus

LOS ALAMOS, New Mexico, March 3, 2010—Two teams of researchers—including Los Alamos National Laboratory theoretical biologists Bette Korber, Will Fischer, Sydeaka Watson, and James Szinger—have announced an HIV vaccination strategy that has been shown to expand the breadth and depth of immune responses in rhesus monkeys. Rhesus monkeys provide the best animal model currently available for testing HIV vaccines.The research appeared in two back-to-back articles in Nature Medicine this week, and outlines a strategy, called “mosaic vaccines,” for reducing the spread of HIV, the virus that causes AIDS. HIV is an extremely variable virus. One of the most daunting challenges for developing an effective HIV vaccine is designing one that stimulates immune responses that will protect an individual from the highly diverse spectrum

of strains of the circulating virus. The mosaic vaccine design uses computational methods developed at Los Alamos to create small sets of highly variable artificial viral proteins. These proteins, in combination, provide nearly optimal coverage of the diverse forms of HIV circulating in the world today.In one of the two papers, Dr. Dan Barouch of Beth Israel Deaconess Medical Center at Harvard University reported very promising results when HIV mosaic vaccines were embedded in specialized vectors —organisms that transmit pathogens to a host—that were designed in his laboratory specifically to make strong “Killer T cell” responses. Killer T cells enable our immune system to recognize and kill virally infected cells, and they help clear or contain viral infections.When this vaccine was used to immunize rhesus monkeys against HIV-1, the most predominant and transmittable type of the virus, the researchers observed up to four-fold improvement in the monkeys’ immune response to HIV-1, compared with natural vaccine strains similar to those that have been used in the past. In the other, complementary study, Drs. Norman Letvin and Sampa Santra, also affiliated with the Beth Israel Deaconess Medical Center, and Dr. Barton Haynes of Duke University, used a distinct HIV mosaic vaccine construct that stimulated an immune response emphasizing “Helper T cells”—the kinds of cells required to stimulate and control many aspects of an immune response. This study also showed an increased breadth and depth of anti-HIV immune responses to the vaccine. Both approaches demonstrated that mosaic vaccines improve the immune response against genetically diverse HIV-1 viruses.“This research indicates that mosaic vaccines represent a promising strategy to expand coverage for genetically diverse pathogens such as HIV-1,” Korber said. “The next step is to see whether the improved immune response found in Rhesus monkeys will hold up in humans, so small-scale human safety and immune response studies are being launched at Harvard and at Duke to explore that possibility.”